FROMMER LAWRENCE & HAUG LLP
745 FIFTH AVENUE NEW YORK, NEW YORK 10151
TEL: (212) 588-0800 FAX: (212) 588-0500

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May 13, 2005

BY FEDERAL EXPRESS

Division of Dockets Management (HFA-305)
Food and Drug Administration
Room 1061
5630 Fishers Lane
Rockville, MD 20852

Re: **Docket No. 2004P-0348;**
Fluticasone Propionate Nasal Spray, 50 mcg

The undersigned petitioner hereby supplements the above-identified Citizen Petition, docketed on August 4, 2004, as follows.

On page 4 of the Petition, petitioner states that the *in vivo* bioequivalence study with a pharmacokinetic endpoint, recommended in FDA's "Draft Guidance for Industry, Bioavailability and Bioequivalence Studies for Nasal Aerosols and Nasal Sprays for Local Action" (April 2003), be conducted as a pre-requisite to approval of all ANDAs for generic formulations of Fluticasone Propionate Nasal Spray, 50 mcg, **at** the maximum labeled adult dose not exceeding the daily recommended dose (emphasis supplied). As set forth in the labeling of the reference listed drug (FLONASE), the maximum labeled dose is 200 mcg (two sprays containing 50 mcg in each spray, sprayed in each nostril), once daily.

This maximum dose level standard is set forth in FDA's April 2003 Nasal Aerosols and Nasal Sprays Draft Guidance, as follows:

> "For an NDA or ANDA, the *in vivo* BE study would be conducted with a replicate or nonreplicate randomized crossover design. For aqueous nasal sprays, the study would be conducted at the maximum labeled adult dose to maximize plasma drug levels, while avoiding the possibility of alteration of the drug deposition pattern within the nose at higher volumes when dosed above label claims." (Guidance, at 26).

FDA's rationale for the maximum dose level standard is:

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CALIFORNIA OFFICE
4660 LA JOLLA VILLAGE DR. SUITE 850 SAN DIEGO, CA 92122
TEL: (858) 731-5000 FAX: (858) 731-5001

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> "The deposition pattern could be altered due to loss of drug from the nasal cavity at these higher volumes, due either to drainage into the nasopharynx or externally from the nasal cavity." *Id.*

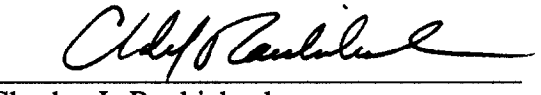
Petitioner re-emphasizes that this maximum dose level standard should be mandatory. Upon information and belief, a sufficiently sensitive assay currently exists (1 pcg/mL) to assess the bioequivalence of fluticasone propionate nasal sprays to the reference listed drug FLONASE in accordance with the protocol prescribed by FDA's April 2003 Draft Guidance.

Therefore, any ANDA applicant who has submitted a bioequivalence studies for Fluticasone Propionate Nasal Spray, 50 mg, which measured bioequivalence using a dose higher than the maximum labeled dose, should be required to repeat the study using the exact maximum labeled dose, to satisfy the reasonable and appropriate standard set forth in the agency's Draft Guidance.

On the other hand, an ANDA for Fluticasone Propionate Nasal Spray, 50 mg, which has demonstrated bio-equivalence to the listed drug at the maximum labeled dose, should be approved at this time. There is no need to await finalization of the Draft Guidance (see original Citizen Petition, p. 5).

Respectfully submitted,

FROMMER LAWRENCE & HAUG LLP

By 
Charles J. Raubicheck

PETITIONER

CJR:bav

cc: Gary J. Buehler, R.Ph. (HFD-600)
Dale P. Conner, Pharm.D. (HFD-650)